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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,784	02/28/2005	Jan Balzarini	50304/061001	8526

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
10/31/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,784	BALZARINI ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28 and 32-38* is/are pending in the application.

4a) Of the above claim(s) *37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-28 and 32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF PRIORITY, IDS, AMENDMENT, RESPONSE TO RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS

1. This application is filed under 35 U.S.C. 371 on 02/28/05 having a filing date of 09/01/03 of PCT/BE03/00144. Acknowledgement is made of Applicant's claim priority based on United Kingdom Application Numbers 0220235.6; 020233.1; 0310890.9 and 0309521.3 having filing dates of 08/30/02; 08/31/02; 04/25/03 and 04/25/03, respectively. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The information disclosure statement (IDS) and Form PTO-1449 filed 12/26/06, the amendment and response to the restriction requirement filed 08/06/07, respectively are acknowledged, entered and considered. In view of Applicant's request claims 32-35, 37 and 38 have been amended and claims 29-31 have been canceled. Claims 23-28 and 32-38 are now pending in the application.

ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group II, claims 29-36, and Compound No. 99 (pg. 48) for Species I, Compound No. 42 (pg. 50) for Species II, Compound No. 53 (pg. 52) for Species III, and *Retroviridae* for Species IV in the communication filed 08/06/07 is acknowledged. The traversal is on the ground(s) that the restriction requirement referring to Groups I (claims 23-28), Group II (claims 32-36) and Group III (claims 37 and 38) is no longer justified after the cancellation of claims 29-31 and the

amendments to claims 32, 37 and 38. Claims 32, 37 and 38 have now been amended to depend from claim 23. Accordingly, the glycopeptides encompassed in claim 23 and amended claims 23, 37 and 38 are the same class of chemical compounds and therefore possess the same technical features and are also closely linked that they should be considered as a single general inventive concept (see M.P.E.P. § 1850). In addition, the International Guidelines provide for Unity of Invention for an independent claim for a given product and an independent claim for use of the product (see M.P.E.P § 1893.03(d)). Accordingly, Applicant contends that it is proper to examine claims 23-28 and 32-38 as one group for further prosecution is noted.

Contrary to Applicant's contention, claim 32 as amended is drawn to a method for preventing a viral infection by administering the compound of claim 23 while claims 37 and 38 are drawn to a method of screening or selecting antiviral compounds or antiviral glycopeptides antibiotics of claim 23 for detecting the antiviral and antibacterial activity and the cell toxicity thereof. Although, both methods use the same compounds (i.e., compounds of claim 23), however, the inventions of both methods as claimed are independent and distinct inventions, and the methods as claimed are different from each other because they represent different technical features and different endeavors (i.e., method of preventing is not the same as assay method of screening or selecting compounds and *vice versa*). Further, the methods differ in material make up, and formulations requiring different reaction condition and effect. Hence, one does not require the other for ultimate use and as such is capable of separate manufacture, use and sale, and is novel and patentable over each other.

Therefore, claims 37 and 38 are withdrawn as non-elected inventions for the reasons of record. Hence, the Office action is directed to the merits of claims 23-28 and 32-36 as *per* elected invention and Applicant is advised to cancel non-elected invention of claims 37 and 38 in the next communication.

The requirement is still deemed proper and is therefore made FINAL.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28 and 32-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instantly claimed invention as claimed in claims 28 and 32-36 is directed to a composition for separate, combined or sequential use in the treatment or prophylaxis of antiviral infections comprising one or more compounds according to claim 23 and one or more compounds effective in treatment or prophylaxis of viral infections, including Retroviral, Flaviviral, Herpes or Coronaviral enzyme or entry inhibitors, in proportions such as to provide a synergistic effect in said treatment or prophylaxis (claim 28) and to

a method for preventing or treating a viral infection in a patient by administering to the patient in need thereof a therapeutically effective amount of one or more glycopeptide antibiotics or derivatives thereof of claim 23 (claims32-36). However, the specification does not enable a method and compositions thereof for the prevention or treatment or prophylaxis of viral infections in general as claimed in claims 28 and 32, and in particular the various families of viral infections and the numerous glycopeptide antibiotics and derivatives thereof in the manner claimed in claims 34-36 and 33, respectively because there are no working examples or data cited in the instant specification, except for the general methods and materials for the preparations of the compounds, representing the structures of the prepared compounds, and determination or evaluation of antiviral and cytostatic/cytotoxic activity of the compounds as exemplified by the Examples and Tables in the instant specification. Example 1 and Tables 1 to 8 represent the structures of the prepared compounds as examples and their respective codes. Example 2 shows general methods and materials for the preparation of the compounds. Examples 3 and 8-13 disclose methodologies for determination of antiviral and cytostatic/cytotoxic activities. Examples 4 and 5 demonstrate evaluations of cytostatic and anti-HIV activities of the compounds. Examples 6 and 7 teach anti-HIV-1 and –HIV-2 activities of some compounds in different cell lines.

Further, the reference of Balzarini et al (all three inventors are authors of this reference) in Antiviral Research, 2006, Vol. 72, pages 20-33 states in the abstract that various semisynthetic derivatives of glycopeptide antibiotics including vancomycin,

eremomycin, teicoplanin, ristocetin A and DA-40926 have been evaluated for their inhibitory activity against feline infectious peritonitis virus (FIPV) and human (SARS-CoV, Frankfurt-1 strain) coronavirus in cell culture in comparison with their activity against human immunodeficiency virus (HIV). On page 21, left column, second paragraph the reference continues by stating that while we could demonstrate that several lipophylic derivatives of the glycopeptide antibiotics, including a variety of aglycon derivatives, showed anti-coronavirus activity in the lower micromolecular range, there was not a close structure-activity relationship for the glycopeptide derivatives against both viruses, suggesting that at least for this particular class compounds, the FIPV cell culture model cannot be regarded as reliable surrogate model to screen for efficient anti-SARS-CoV inhibitors. The fact that the molecular target (peptidoglycan synthesis) for antibacterial activity is entirely absent in viruses and mammalian cells, and the glycopeptide antibiotics are use worldwide for the treatment of infections caused by bacteria, particularly by Gram-positive bacteria.

The reference concludes by stating that some of the compounds inhibited virus infection in the lower micromolar range without measurable cytotoxicity at 80-100 μM. Although the molecular mechanism of anti-HIV and anti-FIPV action is likely to be the viral entry process, no close correlation could be established between the activity of the compounds against HIV-1 and both coronaviruses, or between their activities against SARS-CoV and FIPV. It would appear, therefore, that the FIPV model is not an adequate surrogate model for detecting specific anti-SARS coronavirus inhibitors within the structural class of glycopeptide antibiotics. Further, the instant specification

acknowledges by stating on page lines 19 and 20 that the viral infection remain a major medical problem worldwide because of a lack of therapy, prevention or vaccination strategy and because of the rapid development of resistance.

Therefore, in view of the above, there is no data or activity in the instant specification showing the use of the various claimed compounds for the method of preventing or treating all kinds of viral infections by administering the compounds of claim 23 in the manner claimed in claims 28 and 32-36 in the instant invention. Applicant has not provided even **one example** as claimed, except for the general method and materials for the preparation of the compounds and various *in vitro* assays for the methodologies for determination of antiviral and cytostatic/cytoxic activity in various cell cultures. From this Applicant is attempting to extrapolate to a broad diversity of glycopeptide antibiotics or derivatives thereof for methods of preventing and/or treating all kinds of viral infections in which the effects of the claimed glycopeptide antibiotics and derivatives thereof are unknown for the reasons discussed above, and as such, when this variable is added, the claimed invention becomes little more than conjecture. Moreover, without guidance, the use of various glycopeptide antibiotics and derivatives thereof in general for the prevention/prophylaxis and/or treatment of viral infections in the manner claimed is unpredictable in view of the reference of Balzarini et al as discussed above, and as such, the experimentation left to those skilled in the art is unnecessary and improperly, extensive and undue. See *Amgen Inc. V. Chuqai Pharmaceuticals Co. Ltd.*, 927 F.2d, 1200, 18 USPQ2d 1016

(Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Therefore, the scope of the instantly claimed invention is speculative in claiming a composition for separate, combined or sequential use in the treatment or prophylaxis of antiviral infections comprising one or more compounds according to claim 23 and one or more compounds effective in treatment or prophylaxis of viral infections, including Retroviral, Flaviviral, Herpes or Coronaviral enzyme or entry inhibitors, in proportions such as to provide a synergistic effect in said treatment or prophylaxis (claim 28) and to a method for preventing or treating a viral infection in a patient by administering to the patient in need thereof a therapeutically effective amount of one or more glycopeptide antibiotics or derivatives thereof of claim 23 (claims32-36) for the reasons discussed above.

Furthermore, the first paragraph of 35 U.S.C. 112 requires, *inter alia*, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the

quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, without guidance through working example(s), one of ordinary skill in the art would not predict from *in vitro* assays data disclosed in the instant specification to administer the claimed compounds for prevention and/or treating all kinds of viral infections in patients including humans in the manner claimed in the instant invention in view of the reference of Balzarini et al (3 of authors of the reference are inventors of the instant invention) and in view for the reasons discussed above. Thus, the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention.

CLAIMS REJECTION-35 U.S.C. 112 2nd PARAGRAPH

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 23-28 and 32-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23 and 24 are indefinite in the recitation ".....selected from hydrogen....", "....selected from a group....." and ".....Sug selected from...." because it is not clear if Applicant intends a Markush format. If Applicant intends to use a Markush format, then, the Office recommends the use of the phrase "selected from the group consisting of ....." in listing species to ensure the Markush group is "closed".

Claims 25, 26 and 33 are indefinite and confusing in referring back to code numbers in the description of the application because referring back to a Table or a Figure or a Number is not acceptable claim language. Such material should be incorporated within the claim language. Further, it is long standing Office practice that claims should be completed and self-contained and incorporation into claims by express reference to the specification is not permitted and should not be relied on to define the invention (*Ex parte Fressola*, Bd. Pat. Appl. & Inter., 5/11/93, p. 1608).

Claim 28 recites, "in proportions". It is unclear from the claim and specification as to what extent the compounds may be in proportions and still provide a synergistic effect in said treatment or prophylaxis of antiviral infections, and thus the claim is vague and indefinite.

Regarding claims 28 and 34, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

CITATION OF RELEVANT PRIOR ART

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Balzarini et al (J. Med. Chem., Vol. 46, No. 13, pp. 2755-2764, 2003) demonstrate the antiviral activity of semisynthetic derivatives of glycopeptide antibiotics.

Printsevskaya et al (J. Med. Chem., Vol. 48, No. 11, pp. 3885-3890, 2005) disclose the structure-activity relationship studies of a series of antiviral and antibacterial aglycon derivatives of the glycopeptide antibiotics vancomycin, eremomycin, and decchloroeremomycin wherein removing carbohydrate moieties from the glycopeptides resulted in significant decrease of antibacterial activity.

CONCLUSION AND FUTURE CORRESPONDANCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AAM Mohamed/AAM
October 24, 2007

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